PIPADOR REVISION

MRCOG Part 1 Revision Notes

Glycoprotein Hormones

BIOCHEMISTRY • LECTURE 232

VISUAL EXAMINATION REVISION NOTES

2026 Edition

232

MRCOG PART 1 REVISION NOTES | BIOCHEMISTRY

Glycoprotein Hormones

Structure of LH, FSH, TSH and hCG, glycosylation and half-life, receptors and cross-reactivity, hCG isoforms and clinical use

α + β	β-subunit	Sialic acid	Chr 6 / 19
Heterodimers; α identical	Confers specificity (assays measure β)	↑ Half-life (hCG ≈ 24–36 h)	α gene / LHβ–hCGβ cluster

■ KEY FACTS: Learning objectives

- Describe the structure of the glycoprotein hormones (LH, FSH, TSH, hCG) and the role of glycosylation.
- Describe their receptors and actions, and the basis of cross-reactivity.
- Describe hCG isoforms, assays and clinical applications (pregnancy tests, GTD, screening), and therapeutic gonadotrophins.

232.1 Structure

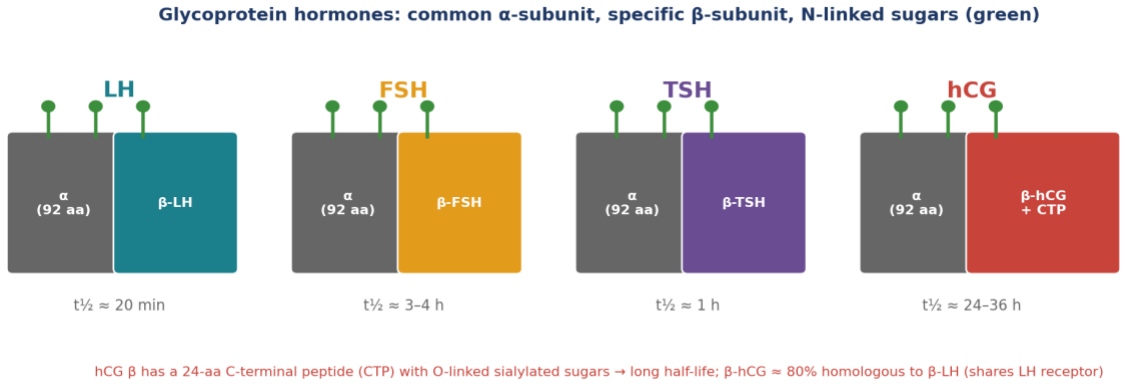


Figure 232.1 — Glycoprotein hormone subunits

- **α-subunit** (92 aa) is **identical** in LH, FSH, TSH and hCG (gene on chromosome 6); **β-subunits** are hormone-specific (FSHβ chr 11; TSHβ chr 1; **LHβ and the hCGβ gene cluster on chromosome 19**).
- Subunits are non-covalently associated; **free subunits are inactive**; both needed for receptor binding.
- **hCGβ** is ≈ 80% homologous to LHβ but has a **24-aa C-terminal peptide (CTP)** with O-linked glycans → **long half-life** and shared **LH/hCG receptor**.
- **Glycosylation** (N- and O-linked; terminal **sialic acid**) determines **circulating half-life** (desialylated forms are cleared by liver asialoglycoprotein receptors), bioactivity and assay detection; FSH isoforms change across the cycle and menopause.

232.2 Receptors and actions

Hormone	Source	Receptor	Main actions
LH	Pituitary gonadotrophs (fast GnRH pulses)	LHCGR (Gs → cAMP)	Theca androgens, ovulation, luteinisation, CL; Leydig testosterone
FSH	Gonadotrophs (slow pulses)	FSHR (Gs)	Granulosa growth, aromatase, inhibin, LH receptor induction; Sertoli function
TSH	Thyrotrophs	TSHR (Gs)	Thyroid hormone synthesis and growth

Hormone	Source	Receptor	Main actions
hCG	Syncytiotrophoblast	LHCGR	Corpus luteum rescue; fetal Leydig testosterone; TSH-like effect at high levels; angiogenesis, immune modulation

Cross-reactivity	Clinical consequence
hCG ↔ TSH receptor	Gestational transient thyrotoxicosis, hyperthyroidism in molar pregnancy/twins, hyperemesis
hCG ↔ LH receptor	IVF hCG trigger (mimics LH surge, ↑ OHSS); hyperreactio luteinalis/theca-lutein cysts; luteoma
hCG ↔ FSH receptor (weak)	Spontaneous OHSS (rare, FSHR mutations)
LH vs hCG in assays	Older tests cross-reacted; modern β-hCG assays specific

232.3 hCG isoforms and clinical use

Form / use	Notes
Intact hCG	Main form in pregnancy; doubles ≈ every 48 h early; peak 8–10 wk
Hyperglycosylated hCG	From invasive cytotrophoblast — early pregnancy, GTN/choriocarcinoma
Free β-hCG	Combined screening (↑ in trisomy 21); some tumours
β-core fragment	Urine metabolite — urine pregnancy tests detect
Pregnancy tests	Urine ≈ 20–25 IU/L (about day of missed period); serum quantitative for PUL (Lecture 183)
GTD	Very high hCG (molar); hook effect with very high levels; serial hCG surveillance after evacuation; hCG-secreting germ cell tumours
Phantom hCG	Heterophile antibodies → false positive serum hCG with negative urine test — avoid unnecessary chemotherapy/surgery

Therapeutic gonadotrophin	Use
Recombinant FSH (follitropin), urinary hMG (FSH + LH activity)	Ovarian stimulation (IVF, ovulation induction), male hypogonadotrophic hypogonadism
hCG (urinary or recombinant)	Final oocyte maturation trigger; luteal support; male hypogonadism, cryptorchidism
Long-acting FSH (corifollitropin — CTP-fused)	Uses the hCG CTP to extend half-life

232.4 Must-know summary

■ EXAM TIP

- LH, FSH, TSH, hCG: **common α**, specific β; heterodimers; GPCRs (Gs/cAMP).
- hCG β has a **CTP** with sialylated O-glycans → half-life ≈ 24–36 h; shares **LH receptor**.
- Sialylation ↑ half-life; desialylated forms cleared by liver.
- hCG cross-reacts with TSHR → gestational thyrotoxicosis; LH receptor → IVF trigger, OHSS.
- Hyperglycosylated hCG → invasive trophoblast/GTN; phantom hCG from heterophile antibodies.

■ MNEMONIC / MEMORY AID

'Same Alpha, Different Beta' — the β tells you which hormone it is.